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10/085,142	03/01/2002	Stephen Glanowski	CL001326	2692

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MILA KASAN, PATENT DEPT.
APPLIED BIOSYSTEMS
850 LINCOLN CENTRE DRIVE
FOSTER CITY, CA 94404

EXAMINER	
SKOWRONEK, KARLHEINZ R	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 04/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/085,142	GLANOWSKI ET AL.	
	Examiner	Art Unit	
	Karlheinz R. Skowronek	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *20-23, 26 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19,24,25 and 28-41* is/are rejected.

7)☒ Claim(s) *2, 12, 13-19, 24-25, and 28-32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *1 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *(4 sheets)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of species 2 (claims 1-41) and species 2-C (claims 24-25) in the reply filed on 12/27/2005 is acknowledged.

Claim Objections

2. Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

3. In the instant case, Claim 2 does NOT further limit claim 1, from which claim 2 depends. Claim 1 is directed to a data point "comprising of at least two numerical values", which indicates the data point could be composed of two or more numerical values, but no less than two numerical values. In comparison, claim 2 is directed to a data point that "comprises two numerical values". The language of Claim 2 indicates said data point could be composed of two or more numerical values, but no less than two numerical values. Since both claims recite the same limitations on the data point, claim 2 does NOT further limit claim 1.

4. Claims 12, 13-19, 24-25, and 28-32 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

5. In the instant case, claim 12 does not further limit claim 11 from which Claim 12 depends. Claim 11 is directed to the determination of a condition exceeding a

predetermined threshold. Whereas, claim 12 is directed to the determination of any condition. The language of claim 12 is broader than the claim from which it depends, claim 11. Therefore, claim 12 does NOT further limit claim 11. Claims 13-19, 24-25, and 28-32 are also objected to because they depend from claim12 and they do not further limit claim 12 to further limit claim 11, therefore contain the same issue due to said dependence.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 1-19, 24-25, and 28-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131

USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 recites the broad recitation a method comprising steps producing a plurality of angular values, sorting data points by angular value, producing a plurality of difference values, determining at least one category-dividing value, and classifying at least one data point to at least one category-dividing value, and the claim also recites an allelic classification method in its preamble which is the narrower statement of the range/limitation. Claims 2-19, 24-25, and 28-32 are also rejected because claims 2-19, 24-25, and 28-32 depend from claim 1, and thus they contain the above issue due to said dependence.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-19, 24-25, and 28-41 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. Claim 1 lacks steps that address treatment of data points in preparation of angular value determination and the process of angular value determination are critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

9. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546

(BPIA 1986) and reiterated by the courts in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of the experimentation necessary, (2) the amount or the direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular Biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for *prima facie* case are discussed below.

10. In the instant case, the methodology for calculation of angular value of a data point is a fundamental step of claim 1. Several operations are performed on the data points after the angular value is calculated such as angular value sorting, determination of angular values difference values, angular value comparison to threshold values and angular value relative classification. If one knew how applicant calculates angular value, one would be able to implement the method of claim 1. It is unknown, by the written description given, how to calculate the angular value. From the language of claim 1, one can only guess what the method by which the angular values are calculated. The specification superficially indicates that the angular value is an arctangent of the data point (pg. 7, line 8-9). However, it unknown what constitutes the reference point for the purpose of calculating the arctangent angular value. Angular data for any data point could be calculated from a random data point chosen to be the reference point relative

to any other data point in the data set. Angular value is calculated from the data set data point values as described by the specification, but relative to a random reference point.

11. The drawings included with the specification suggest the data points may be plotted in a Cartesian coordinate system. One could, with equal ease plot the data points in a polar coordinate system. The extra step of plotting the data points in a polar coordinate system, by well known mathematical transformation, requires the calculation of an angular value (θ) equal to the arctangent of the ratio the Y-axis coordinate value (Y) to the X-axis coordinate value (X) ($\theta = Arc\tan\left(\frac{Y}{X}\right)$) and calculating the Euclidian distance (d) from the origin equal to the square root of the X-axis coordinate value squares plus the Y-axis coordinate value squared ($d = \sqrt{X^2 + Y^2}$). Although the specification does not indicate so, data point plotting forms an essential step in the method of claim 1. The Non-Patent Literature included with the application further indicates the conversion from Cartesian coordinates to polar coordinate system is an essential step of the method (pg. 37, Heil, et al. Pacific Symposium on Biocomputing. 01/03-07/2002.). However, claim 1 does not define any coordinate system interconversion nor does the specification. The omission of an essential step of the method renders the method of claim 1 unpredictable and thus would require undue experimentation. Claims 2-19, 24-25, and 28-32 are also rejected because claims 2-19, 24-25, and 28-32 depend from claim 1, and thus they contain the above issue due to said dependence.

12. In the instant case, the preparation of the data for angular value determination is also an essential step of claim 33. Claim 33 is directed to an allelic differentiation method comprising acquiring fluorescence data for plurality of samples, generating angular data for each sample, arranging samples by angular value, determining a difference value for each sample, association of a difference value range with an allelic composition, evaluating each sample's difference value in relation to a difference value range, and identifying the allelic composition of the sample based on the difference range. For the reasons cited above for the lack of enablement for claim 1, omission of the steps essential to calculating a data point's angular value in claim 33 also results in a lack of enablement of claim 33. Claims 34-38 are also rejected are also rejected because claims 34-38 depend from claim 33, and thus they contain the above issue due to said dependence.

13. In the instant case, the preparation of the data for angular value determination is also an essential step of claim 39. Claim 39 is directed to a methods of genotypic analysis comprising amplification a plurality of genetic samples, calculating a angular value for each sample, ordering the samples by angular value, calculating a difference value for each sample, identifying difference value ranges that correspond to homozygous or heterozygous variations, and determining whether a sample corresponds to homozygous or heterozygous allelic variants. Claim 39 recites "calculating angular values for each sample by comparing intensity information for the at least two labels". For the reason cited above for claim 1, omission of the steps essential to calculating a data point's angular value in claim 39 also results in a lack of

enablement of claim 39. Claims 40-41 are also rejected are also rejected because claims 40-41 depend from claim 39, and thus they contain the above issue due to said dependence.

14. Claims 33-38 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. Claim 33 lacks steps to relate data of an unknown allelic composition to data for which the allelic composition is known for the purposes of determining a difference value range associated with an allelic composition which is critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

15. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPIA 1986) and reiterated by the courts in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of the experimentation necessary, (2) the amount or the direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular Biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for *prima facie* case are discussed below.

16. In the instant case, claim 33 is directed to associating a difference value range with an allelic composition. Essential to associating a difference range to an allelic composition is the establishment of a reference allelic composition. In the absence of reference data, how are difference value ranges determined? Once a difference value range is determined, how does one relate the difference range to an allelic composition in the absence of reference data? If reference data is not required, then the steps to determine difference ranges should be disclosed. Are difference ranges determined by the analysis of a matrix of difference values for all data point in the data set? The specification does not recite the matter of how difference values are used to generate difference ranges that correspond to specific allelic compositions. If one knew how to determine a difference value ranges for the purpose of correlating said range to allelic compositions, one would be able to able to identify difference values that correspond to specific allelic compositions. Because there are many ways one could determine a difference value range to associate with an allelic composition, determining a difference value range becomes unpredictable and would thus require undue experimentation. Claims 34-38 are also rejected because they depend from claim 33, and thus they contain the above issue due to said dependence.

17. Claims 39-41 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. Claims 39-41 lack the steps that address treatment of data points in preparation of angular value determination, the process of angular value determination and steps to relate data of an unknown allelic composition to data for which the allelic composition is known for the purposes of determining a difference

value range associated with an allelic composition that are critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

18. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPIA 1986) and reiterated by the courts in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of the experimentation necessary, (2) the amount or the direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular Biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for *prima facie* case are discussed below.

19. The arguments against claim 39 are the same as the arguments against claim 33. Claim 39 claims limitations that are not disclosed in the specification. As outlined for claims 1 and 33, the lack of direction by the specification for claim 39 make the determination of angular values and difference ranges unpredictable and would thus require undue experimentation. Claims 40-41 are also rejected because they depend from claim 39, and thus they contain the above issue due to said dependence.

20. In the instant case, claim 39 is directed to method comprising amplifying a plurality of genetic samples, calculating a angular value for each sample, ordering the samples by angular value, calculating a difference value for each sample, identifying difference value ranges that correspond to homozygous or heterozygous allelic variations and to determining whether or not a sample is homozygous or heterozygous by assigning the sample's difference value to a difference value range corresponding to the specific allelic variation. The specification describes a category dividing value;

> **"A difference value is then calculated for each data point by subtracting the angular value of the previous datapoint from that of the current data point. The difference value of the first data point is that point's angular value.**
>
> **If the difference value is large enough to exceed a predetermined threshold, a new category-dividing value is designated between the two angle values from which that difference value was calculated (pg. 7, lines 10-15)".**

However, nowhere in the specification is a basis provided indicating the identification of difference value ranges and relation of said ranges to an allelic variation. Additionally, the disclosure does not provide a basis for how the determined difference ranges correspond to homozygous and heterozygous allelic variations. Do a set of criteria exist that correspond a given difference range to an allelic variation? How are the criteria determined?

21. Claims 36 and 39-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

22. In the instant case, claim 39 is directed to a method of amplifying a plurality of genetic samples. The disclosure provides no basis for amplifying a plurality of genetic samples. How does an algorithm amplify a genetic sample or even a single genetic sample? The amplification of any number of genetic samples by a method such as polymerase chain reaction requires the physical manipulation of physical compounds but also requires a materially different device from a computational device, a device that manipulates values. Claims 40-41 are also rejected because of their dependence from claim 39, and thus contain the above issue due to said dependence.

23. In the instant case, claims 36 and 40 are directed to normalizing the angular values. The specification does NOT recite that angular values are normalized at any point or before a difference value is determined. Is angular value normalization essential to the method disclosed? Would one be able to practice the method if angular values are not normalized? How would the lack of normalized angular values effect the outcome of the method? The lack of written description for normalizing angular values illustrates the disclosure does not reasonably convey the inventor had possession of the claimed invention. Claim 41 is also rejected because of its dependence from claim 40, and thus it contains the above issues due to said dependence.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karlheinz R. Skowronek whose telephone number is (571) 272-9047. The examiner can normally be reached on Mon-Fri 8:00am-5:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Ardin H. Marschel 4/3/06
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER